

CLAIMS

1. A method for producing immortalised antibody-secreting cells, comprising:

- (a) providing a transgenic animal having antibody-secreting cells capable of expressing one or more transgenes, wherein the antibody-secreting cells are in a non-immortalised state in the absence of a stimulus and are capable of changing to an immortalised state by means of the transgene or transgenes upon exposure of the cells to the stimulus;
- (b) extracting the antibody-secreting cells from the animal; and
- (c) exposing the antibody-secreting cells to the stimulus, thereby immortalising the antibody-secreting cells by means of the transgene or transgenes.

2. A method for producing antibodies, comprising producing immortalised antibody-secreting cells by a method as defined in claim 1, and collecting antibodies from the cells.

3. A method for preparing a clonal population of immortalised cells which produce a monoclonal antibody, comprising:

- (a) providing a transgenic animal having antibody-secreting cells capable of expressing one or more transgenes, wherein the antibody-secreting cells are in a non-immortalised state in the absence of a stimulus and are capable of changing to an immortalised state by means of the transgene or transgenes upon exposure of the cells to the stimulus;
- (b) extracting the antibody-secreting cells from the animal;
- (c) exposing the antibody-secreting cells to the stimulus, thereby immortalising the antibody-secreting cells by means of the transgene or transgenes;

(d) selecting an immortalised antibody-secreting cell which produces the antibody; and

(e) preparing the clonal population of immortalised cells from the immortalised antibody-secreting cell.

4. A method according to any preceding claim, wherein expression of a transgene in the antibody-secreting cells is under the control of an inducible promoter, and the stimulus is capable of regulating activity of the promoter and transgene expression.

5. A method according to claim 4, wherein the stimulus promotes promoter activity and transgene expression.

6. A method according to claim 4, wherein the stimulus inhibits promoter activity and transgene expression.

7. A method according to any preceding claim, wherein a product of a transgene in the antibody-secreting cells promotes immortalisation in the presence of the stimulus, and does not promote immortalisation in the absence of the stimulus.

8. A method according to any of claims 1 to 5 or claim 7, wherein the transgene is an oncogene.

9. A method according to claim 8, wherein the oncogene is a gene for the large T antigen.

10. A method according to any of claims 1 to 5 or claims 7 to 9, wherein the transgenic animal is an immortomouse.

11. A method according to any of claims 1 to 4 or claim 6, wherein a product of a transgene in the antibody-secreting cells inhibits immortalisation in the absence of the stimulus, and does not inhibit immortalisation in the presence of the stimulus.

12. A method according to claim 11, wherein the transgene is a tumour suppressor gene.

13. A method according to any of claims 1 to 5 or 7 to 9, wherein a product of a transgene in the antibody-secreting cells inhibits a tumour suppressor function in the cells.

14. A method according to claim 13, wherein the transgene is mdm2.

15. A method according to claim 13, wherein the transgene comprises cre recombinase, the tumour suppressor function results from a tumour suppressor gene, and the tumour suppressor gene, or a functional part thereof, is flanked with loxp sites.

16. A method according to claim 13, wherein a product of the transgene comprises an antisense RNA or ribozyme RNA which is capable of inhibiting expression of a tumour suppressor gene.

17. A method according to any of claims 12 to 16, wherein the tumour suppressor gene or tumour suppressor function comprises p53.

18. A method according to claim 8, wherein the oncogene comprises myc, abl, bcl-2, v-rel, ras, papillomavirus E6 protein, papillomavirus E7 protein, adenovirus E1A, PIM1, RhoH/TTF or PAX5.

19. A method according to any preceding claim, wherein the transgenic animal comprises antibody-secreting cells in which a tumour suppressor gene has been deleted.

20. A method according to any preceding claim, wherein the method comprises the further step of immunising the transgenic animal with an antigen before step (b).

21. A method according to claim 20, wherein step (d) comprises selecting an antibody-secreting cell which produces an antibody which recognises the antigen.

22. A method according to any of claims 3 to 22, wherein step (d) comprises fluorescence activated cell sorting.
23. A method according to any of claims 1 to 19, wherein the transgenic animal is not immunised.
24. A method according to any preceding claim, wherein the stimulus comprises a temperature change.
25. A method according to any preceding claim, wherein the stimulus comprises a chemical stimulus.
26. A method according to any preceding claim, wherein the antibody-secreting cells comprise B lymphocytes.
27. A method according to any preceding claim, wherein the antibody is a humanised antibody.
28. A method according to any preceding claim, comprising a further step of storing the antibody-secreting cells at a temperature of 0°C or below, after extracting the antibody-secreting cells from the animal, and before or after exposing the antibody-secreting cells to the stimulus.
29. A method for producing a monoclonal antibody, comprising producing a population of immortalised cells by a method as defined in any of claims 3 to 28, and producing the monoclonal antibody from the population of immortalised cells.
30. A clonal population of immortalised antibody-secreting cells obtained by a method as defined in any of claims 3 to 28.
31. A monoclonal antibody obtained by a method as defined in claim 29.

32. An isolated, immortalised antibody-secreting cell derived from a transgenic animal, wherein the cell expresses one or more transgenes, the cell is capable of being maintained in an immortalised state by means of the transgene or transgenes in the presence of a stimulus, and the cell is capable of changing to a non-immortalised state in the absence of the stimulus.

33. An isolated clonal population of immortalised antibody-secreting cells which produce a monoclonal antibody, comprising a population of immortalised antibody-secreting cells as defined in claim 32.

34. Use of a transgenic animal for producing immortalised antibody-secreting cells, wherein the transgenic animal has antibody-secreting cells capable of expressing one or more transgenes, and wherein the antibody-secreting cells are in a non-immortalised state in the absence of a stimulus and are capable of changing to an immortalised state by means of the transgene or transgenes upon exposure of the cells to the stimulus.

35. Use of a transgenic animal for producing an antibody, wherein the transgenic animal has antibody-secreting cells capable of expressing one or more transgenes, and the antibody-secreting cells are in a non-immortalised state in the absence of a stimulus and are capable of changing to an immortalised state by means of the transgene or transgenes upon exposure of the cells to the stimulus, and the transgenic animal is used to provide immortalised antibody-secreting cells capable of producing the antibody.